



vehicle

cmpd 15

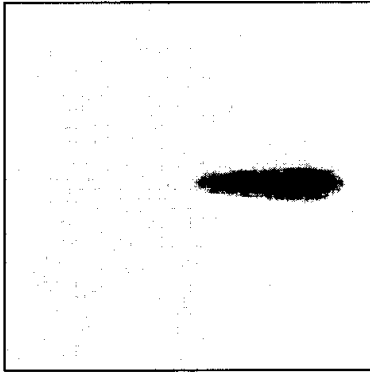


FIG. A -- Compound 15 increases MCIP1 protein expression. Western blot with anti-MCIP1 antibody. Protein prepared from neonatal rat ventricular myocytes exposed to vehicle (DMSO) or compound 15 (10 μ M) for 48 hours.

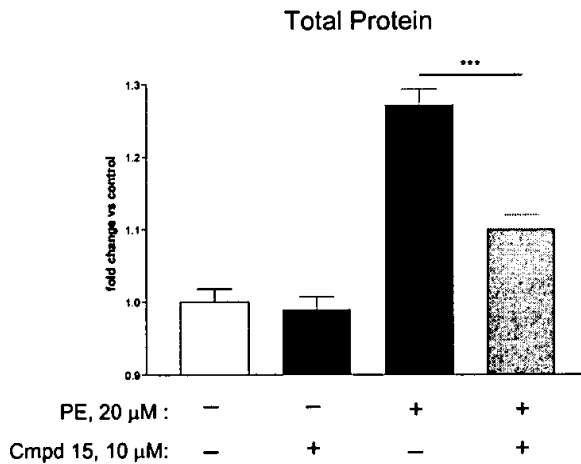


FIG. B -- Compound 15 attenuates phenylephrine-induced increases in total protein. Total protein was measured in neonatal ventricular myocytes exposed to the hypertrophic agonist phenylephrine and compound 15 for a period of 48 hours.

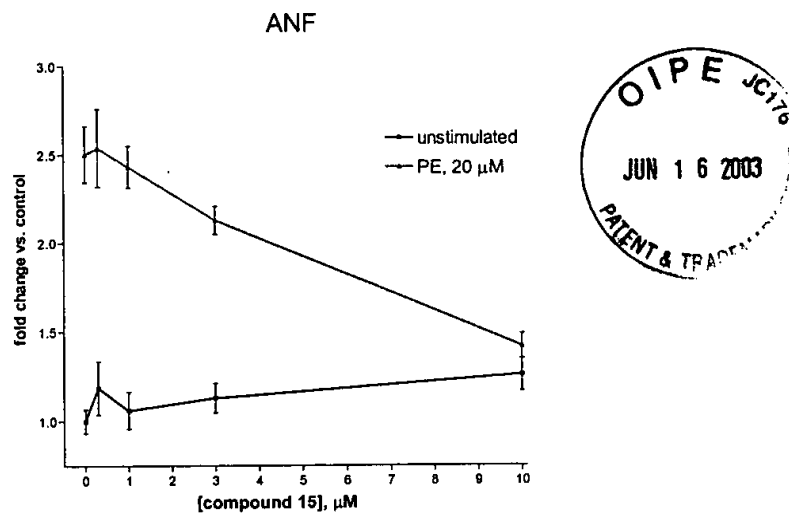


FIG. C -- Compound 15 attenuates phenylephrine-induced increases in secreted ANF. Secreted ANF was measured in neonatal ventricular myocytes exposed to the hypertrophic agonist phenylephrine and compound 15 for a period of 48 hours

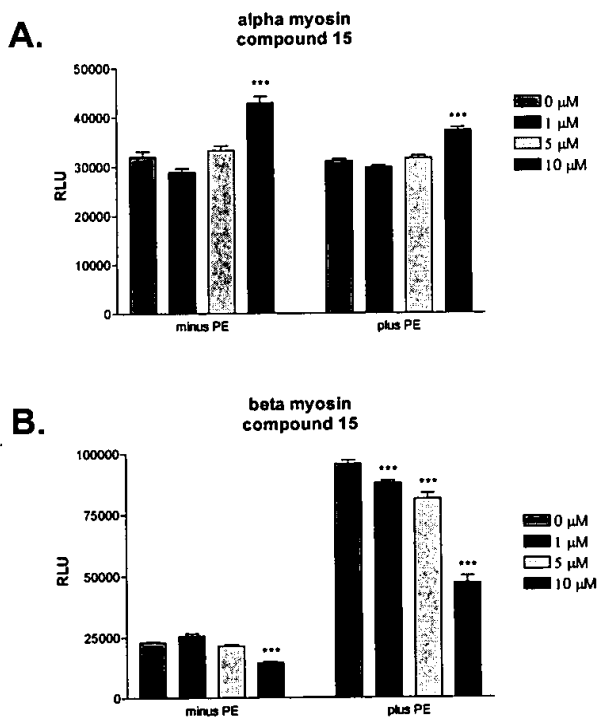


FIG. D -- Compound 15 reverses hypertrophic changes in myosin heavy chain isoform expression in cardiac myocytes. A) Alpha myosin heavy chain expression in neonatal rat ventricular myocytes in the presence or absence of phenylephrine and treated with three concentrations of compound 15. B) Beta myosin heavy chain expression.

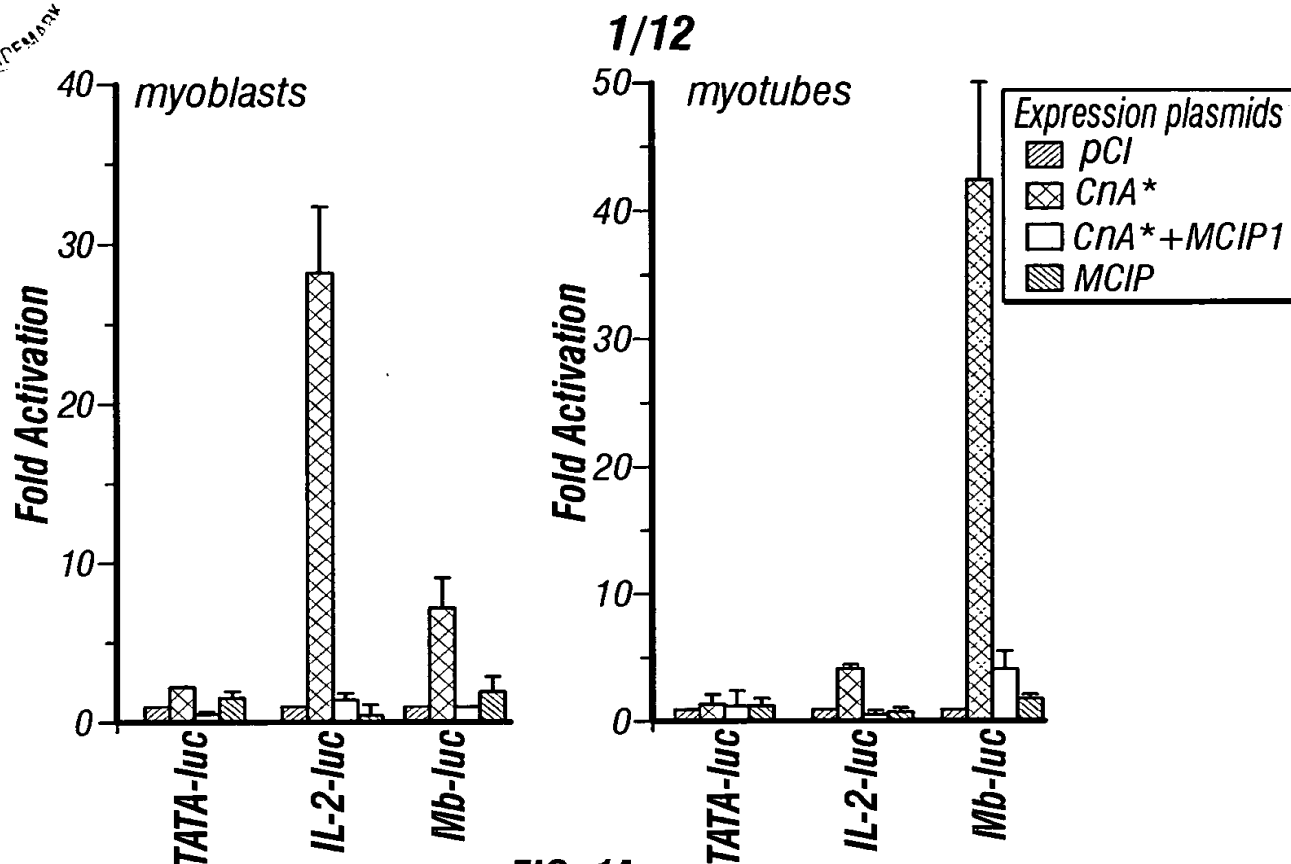
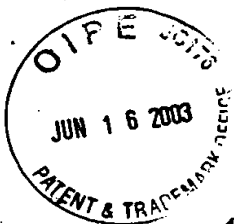


FIG. 1A

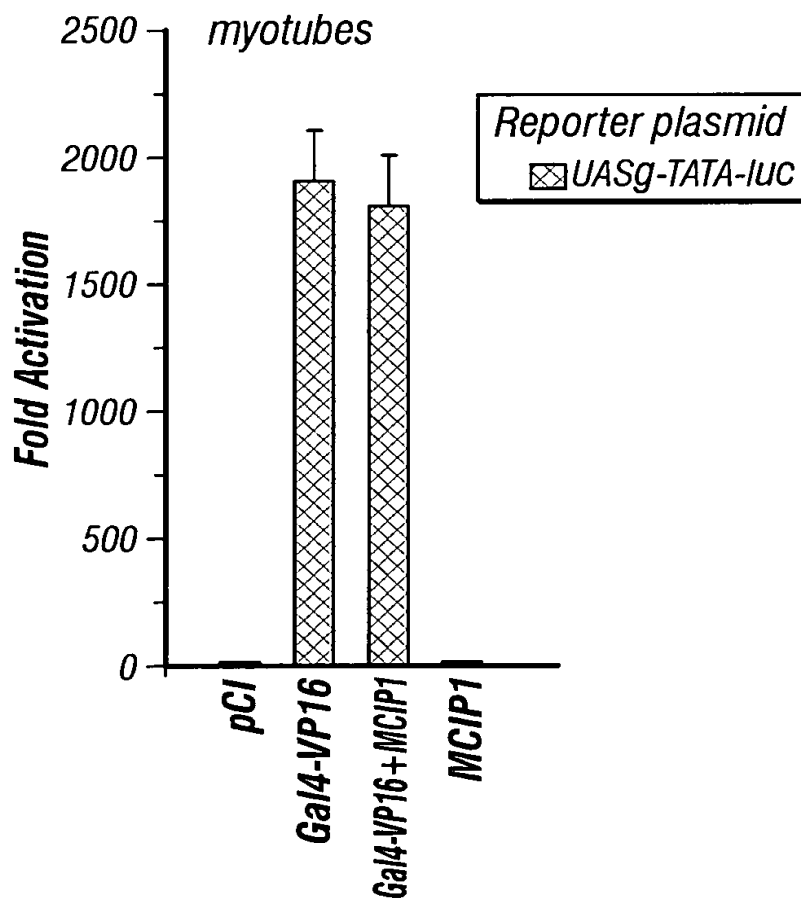


FIG. 1B



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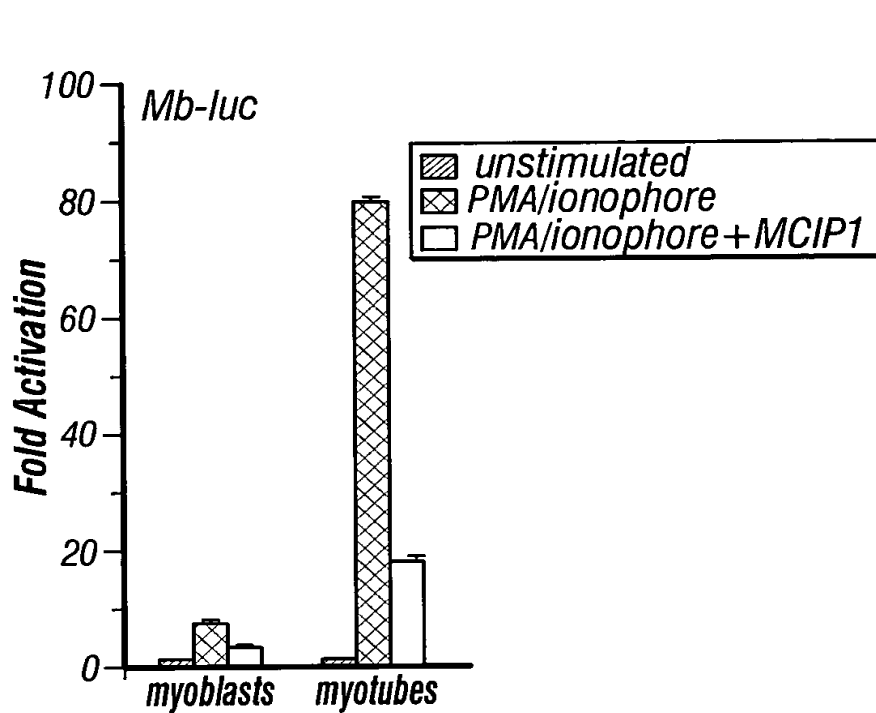


FIG. 2A

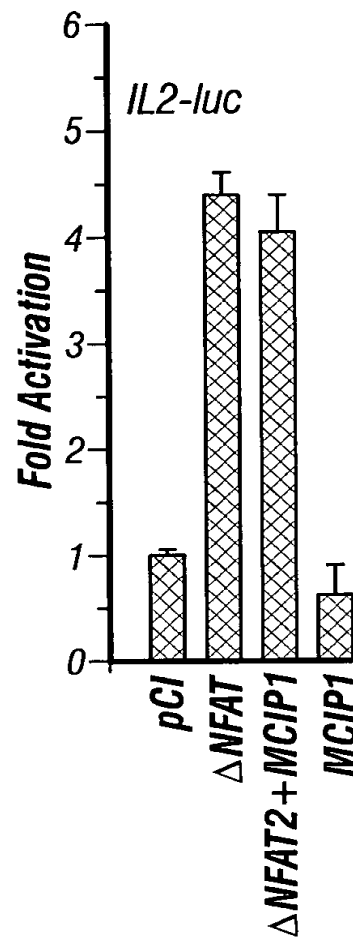


FIG. 2B

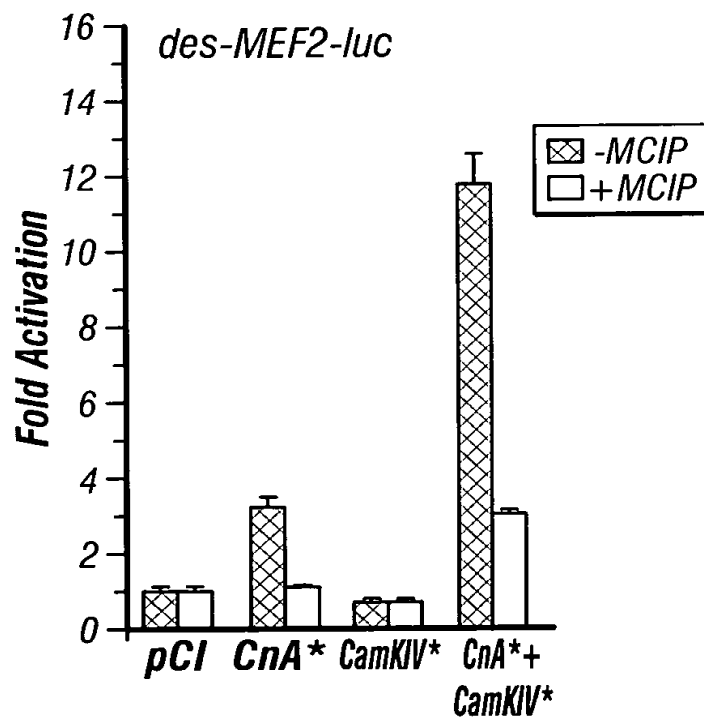


FIG. 2C

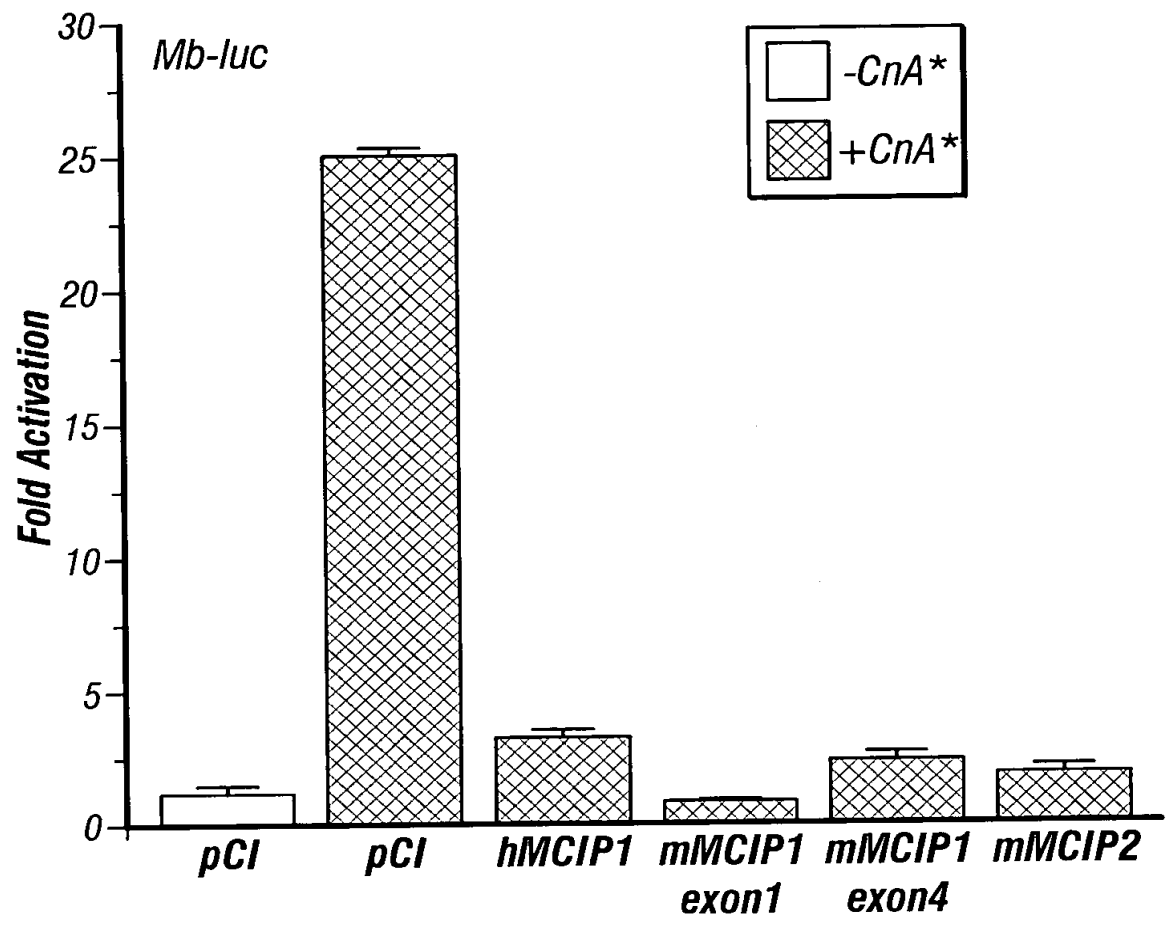


FIG. 3



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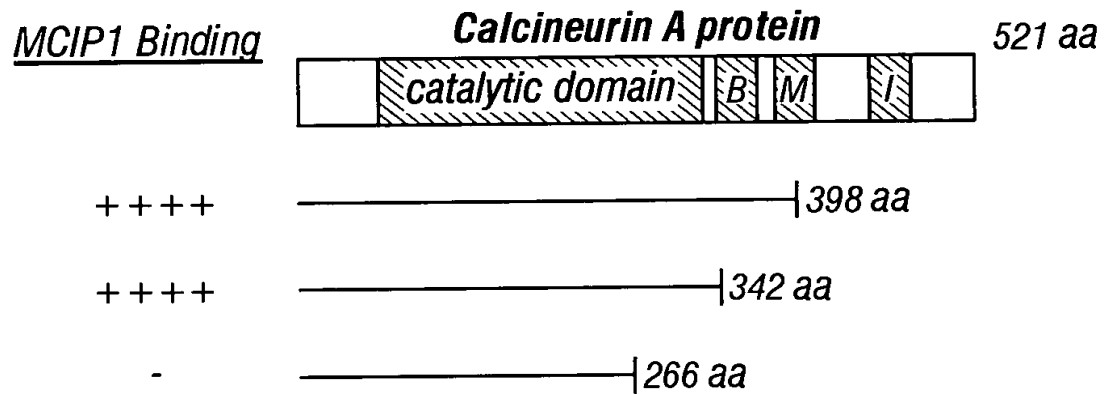


FIG. 4A

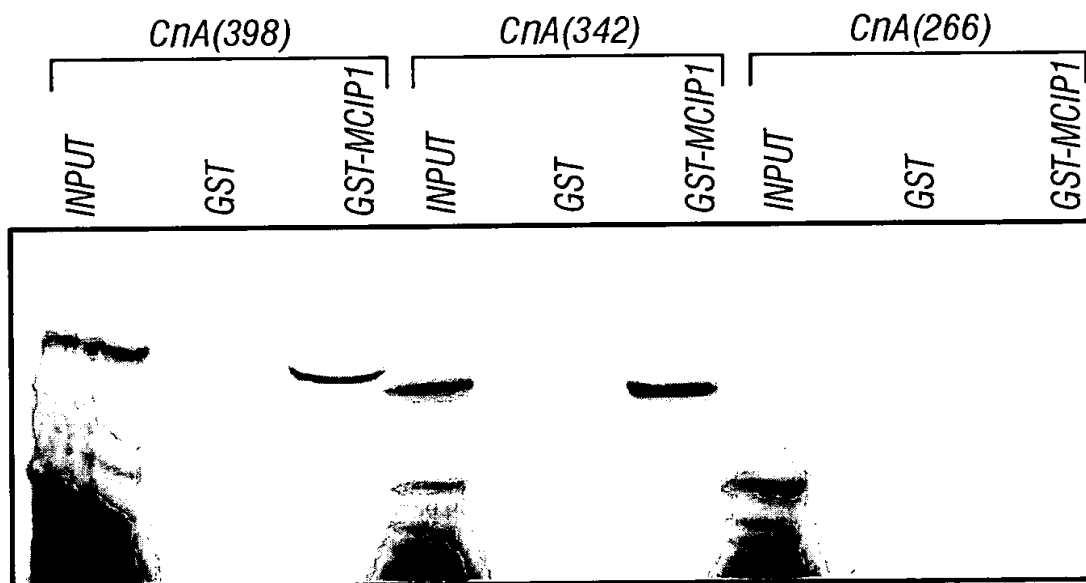


FIG. 4B



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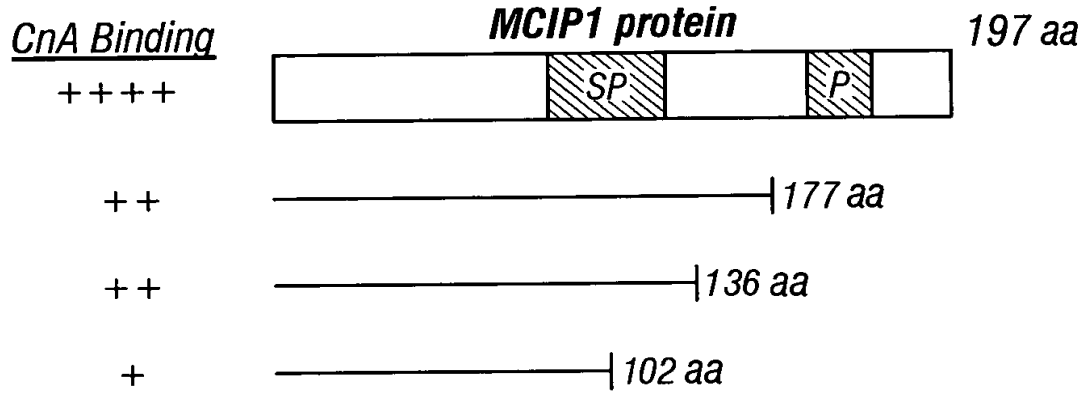


FIG. 5A

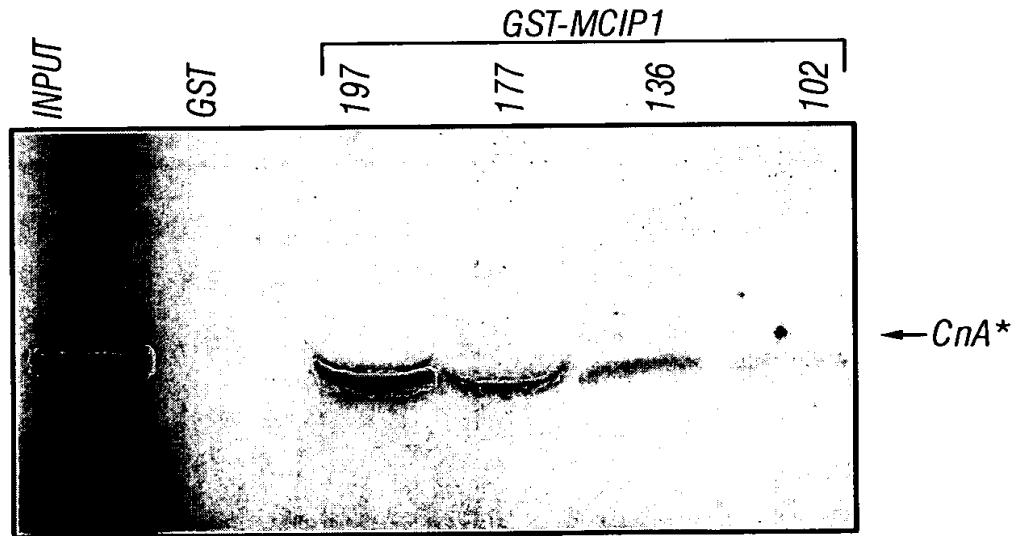


FIG. 5B

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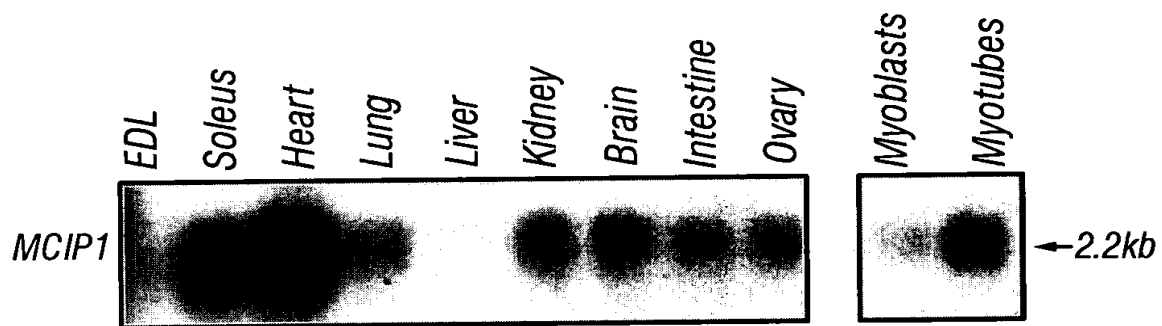


FIG. 6A

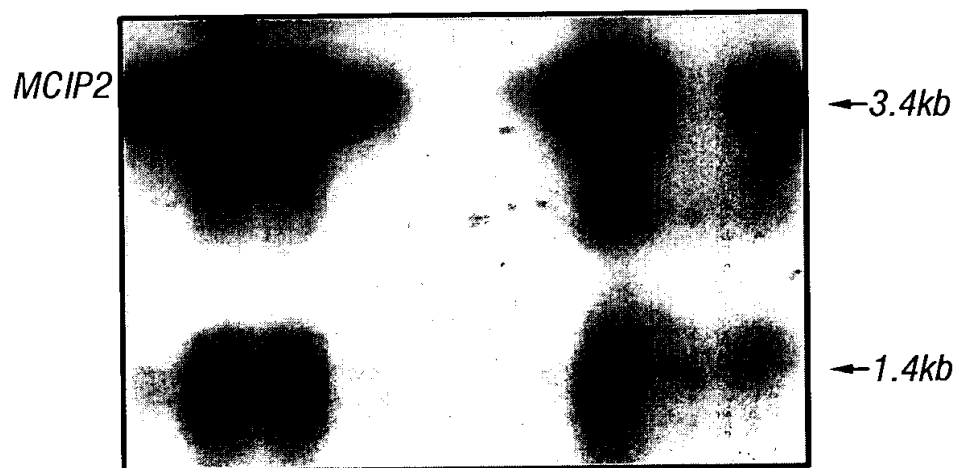
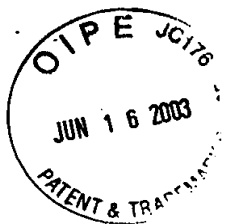


FIG. 6B



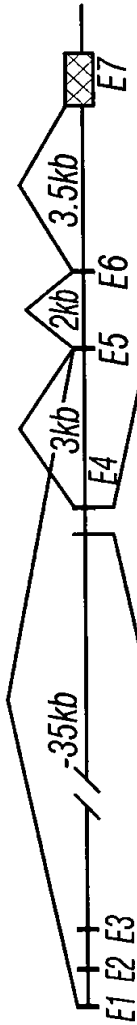
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<i>Rank</i>	<i>Fold</i>	<i>Gene</i>	<i>Genbank ID</i>
<i>hypertrophic α-MHC-CnA* vs. wild-type</i>			
1	8.1	Calcineurin-A	AA245461
2	4.0	ANF precursor type B	AA030805
3	3.3	ANF precursor type A	W14325
4	3.1	sk mus LIM protein (FHL1)	AA047966
5	3.0	OSF-2	W81878
→ 6	2.7	MCIP-1	AA200984
7	2.7	EST (mouse)	AA110791
8	2.3	MCPSF (Mouse cleavage and polyadenylation factor)	AA221269
<i>failing α-MHC-CnA* vs. hypertrophic α-MHC-CnA*</i>			
1	3.3	Procollagen XV	W83331
2	2.9	OSF-2	W81878
3	2.8	EST (mouse)	AA124355
4	2.7	Alpha-crystallin	AA231358
→ 5	2.5	MCIP-1	AA200984
6	2.2	Procollagen III	W89883
7	2.1	p53BP2	AA467287
8	2.1	Calcineurin-A	AA245461

FIG. 7



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-874 CAAC CTCGGCATA AATGGGTAA
-850 TGCCTCTTTG CTCAGTTTCA AAGCTAGAT TGCTCAGTTT CAAAGGCTAG
-800 TGTTTTTGTA TCCTTTGCCCT GAATTCGTGA GTGCTTTGAA AATGATCGAA
-750 GTGTTTCATA TCCCCAGTTC TCAAATTATA ATAATGAAGT TTICAAATGA
-700 AAATCCTAGG ATTGTTTTAG GTTCTGTTG CTCCATTCCA CTGTGGGATA
-650 CAAGTAGAAA TTGGGACATT CATCCAATAA AATGTCACTG GGGAAAAAAA
-600 TTTTAACIAC ACTTCAAAAT CATTCCTCTT TTTGTCCCTT AAAATTTTTA
-550 TTGACCAAGA CAGATTTCAA AATGTTTTCT CTAATACCCC AAAGTGAAAC
-500 TTTGATTGAG GTTTTCAGGA AATTCAGGG ATCAAGTATG TCACCCCGGAC
-450 TTIGGTTTCC AGGTTTCCCA AAGTCTTGAA ATTTCCCTAC AGTCTAATTG
-400 CTGTTTATTG CCACAGACCT TCATCCTTTT TCTTTTGTA CAITTTCCAI
-350 CTAAAGAAGG GTCGTCCCAT TCGGCCGAGG AGCGTGTGT CTGAGTAGCT
-300 GAATGGAATT ACTACGAGTG GAAACTATGC TGAAGAGAG GTTGATAAAG
-250 CAGCTGTCAA GCAAACCTCA GCTGTTTTT CCATCTCCC CAAGCAAAGT
-200 TAATTAGCAT AGGAAAATG ACTAAGGTGT TGACGTCAAC TCTTTCCAGT
-150 AGAAACTTAC ACTTTGTCCC TGCTACCTG CAAGCATCCA CGACTTGACT
-100 CAGGAATTTG CTGTCCAAAC AGGATGCTGT GGAAGCTGCA CTTTTTTTTT
-50 CCCCAGGGAG TGGGGGCTGG CCCTTACTGC TTTATAAGCA CCAGCTCAAG
+1 AAGGAACCTA CAGCTCTTG GAAAGGAAT

FIG. 8A



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MCIP exon 4 promoter constructs

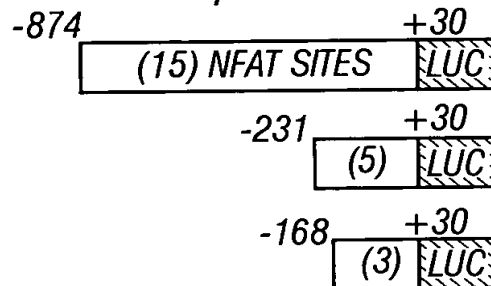


FIG. 8B

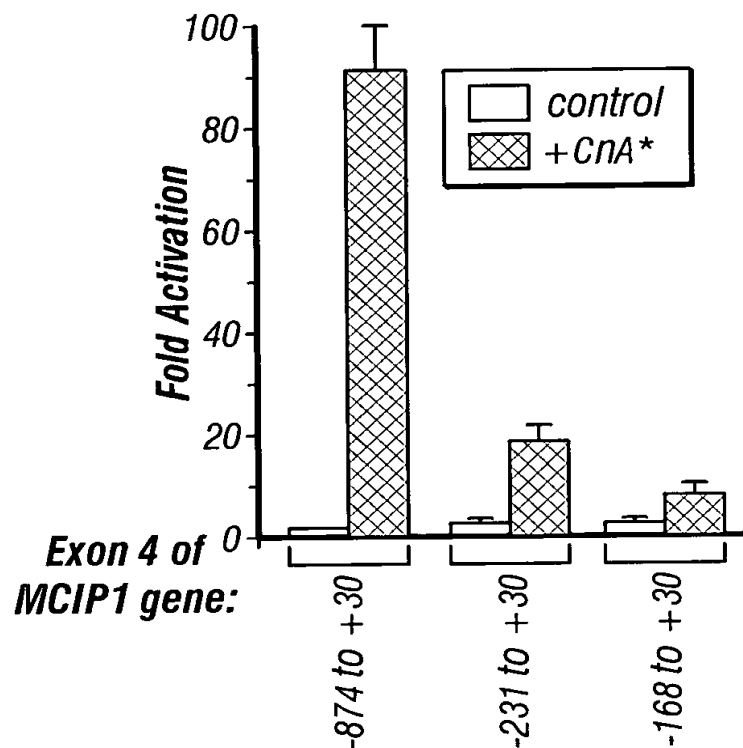


FIG. 8C



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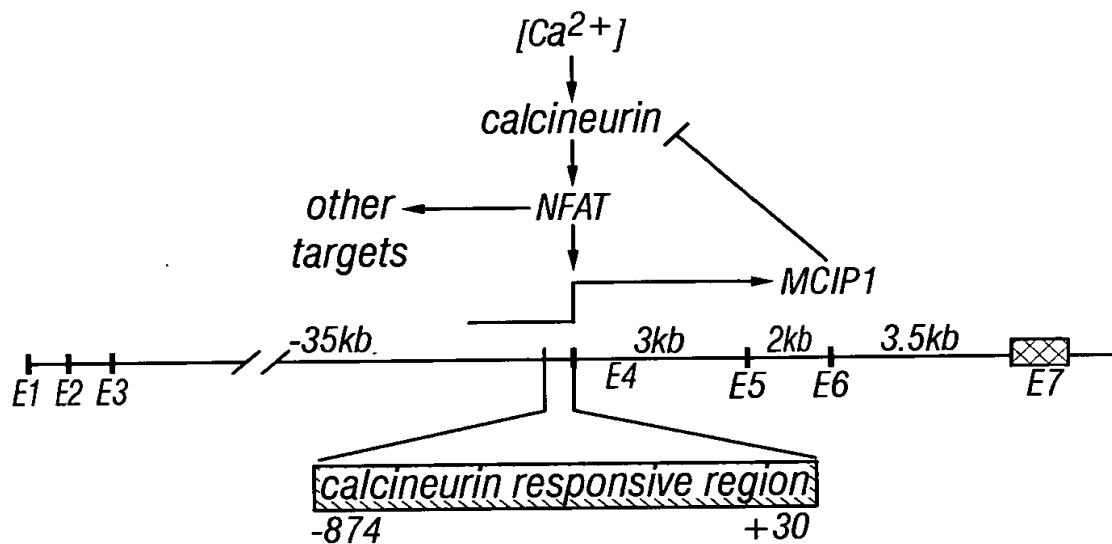


FIG. 9

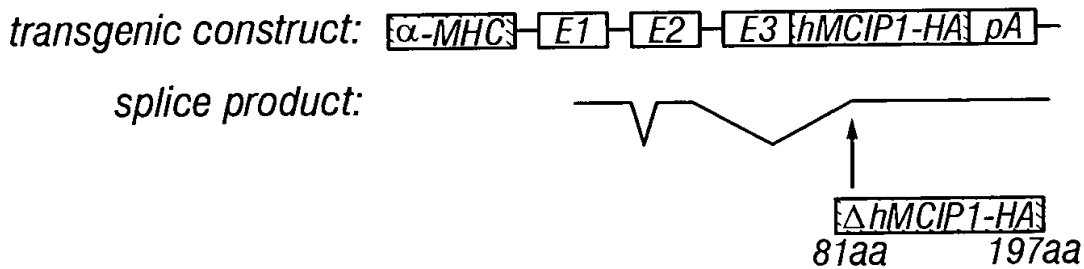
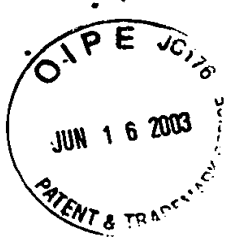


FIG. 10



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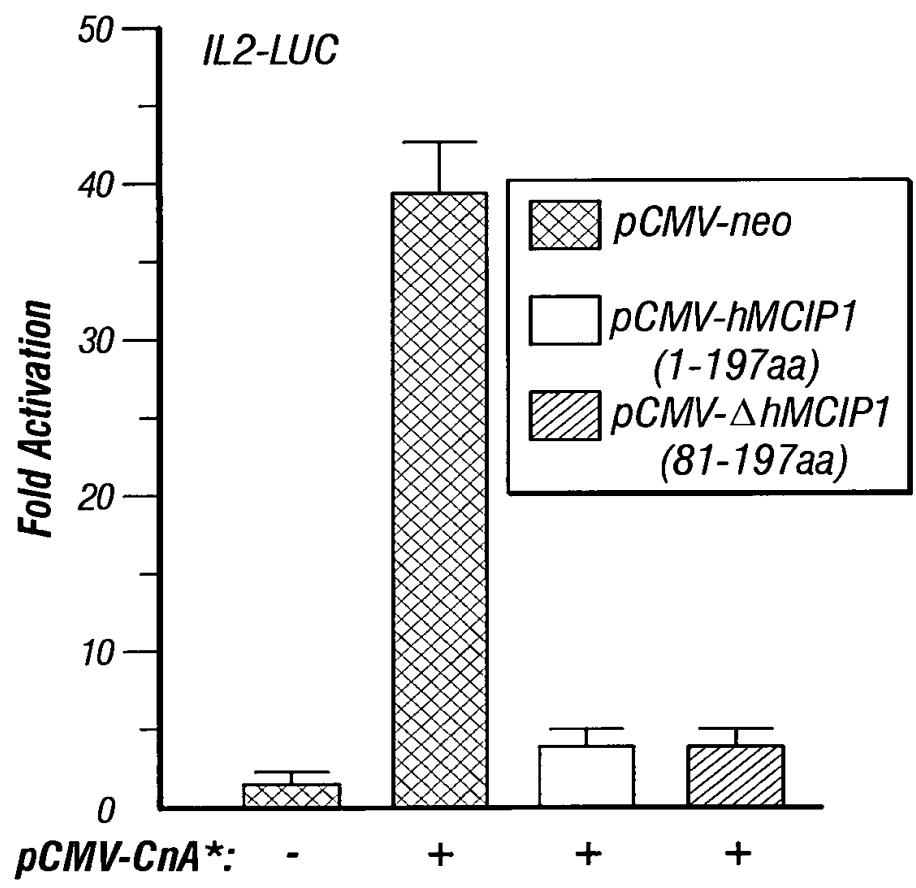
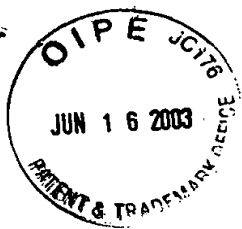


FIG. 11



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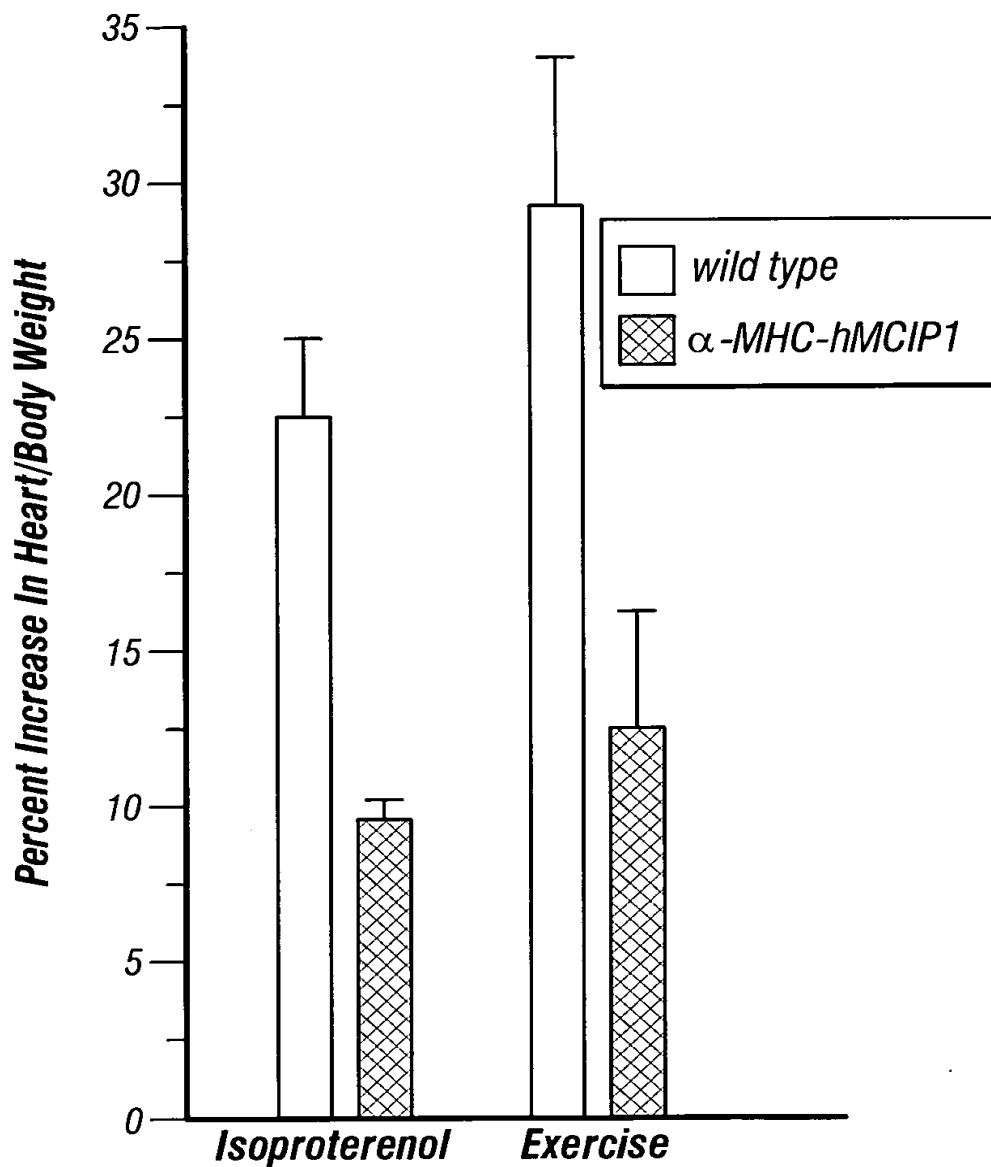


FIG. 12